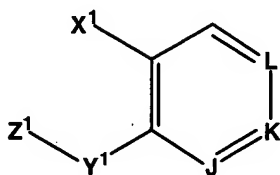


CLAIMS

What is claimed is:

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof:
wherein the compound of Formula (I) is:

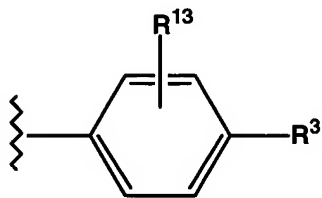


I

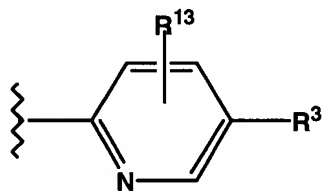
wherein:

X¹ is:

(a)

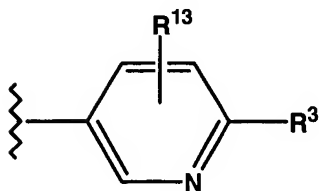


(b)



or

(c)



Y¹ is:

(a) $-(CR^1R^2)_a-$;

- (b) $-(\text{CR}^1\text{R}^2)_b\text{-A}^1\text{-}$;
- (c) $-\text{A}^1\text{-(CR}^1\text{R}^2)_b\text{-}$;
- (d) $-\text{CR}^1\text{R}^2\text{-A}^1\text{-CR}^1\text{R}^2\text{-}$; or
- (e) $-\text{CR}^1=$;

5 Z^1 is:

(a) mono-, di- or tri-substituted phenyl or 2-naphthyl, wherein the substituents are each independently:

- (1) hydrogen;
- (2) halo;
- (3) lower alkyl;
- (4) haloalkyl;
- (5) alkylthio;
- (6) $-\text{NR}^4\text{R}^5$;
- (7) $-\text{C}(\text{O})\text{-lower alkyl}$;
- (8) $-(\text{CH}_2)_a\text{-C}(\text{O})\text{O-R}^6$;
- (9) $-\text{OR}^{11}$; or
- (10) $-(\text{CR}_e\text{R}_f)_q\text{-U-V}$

(b) mono-, di- or tri-substituted cycloalkyl or heterocyclic ring, wherein the substituents are each independently:

- (1) hydrogen;
- (2) halo;
- (3) lower alkyl;
- (4) haloalkyl;
- (5) alkylthio;
- (6) $-\text{NR}^4\text{R}^5$;
- (7) $-\text{C}(\text{O})\text{-lower alkyl}$;
- (8) $-(\text{CH}_2)_q\text{-C}(\text{O})\text{O-R}^6$;
- (9) $-\text{OR}^{11}$;
- (10) $-(\text{CR}_e\text{R}_f)_q\text{-U-V}$;
- (11) oxo; or
- (12) thial;

(c) alkyl;

and the bond between Y^1 and Z^1 may be a single bond or a double bond such that the valencies are satisfied;

A^1 is:

- 5 (a) oxygen;
(b) thio;
(c) sulfinyl;
(d) sulfonyl; or
(c) $-N(R^{12})-$;

10 $-J=K-L=$ is:

- (a) $-CR^7=N-CR^8=$;
(b) $-CR^8=N-CR^7=$;
(c) $-N=N-CR^7=$;
(d) $-N=N-CR^8=$;
15 (e) $-CR^7=N-N=$;
(f) $-CR^8=N-N=$;
(g) $-N=CR^7-N=$; or
(h) $-N=CR^8-N=$;

R^1 and R^2 are each independently:

- 20 (a) hydrogen;
(b) lower alkyl;
(c) substituted lower alkyl;
(d) lower alkoxy;
(e) lower haloalkyl; or
25 (f) halo; or

R^1 and R^2 taken together are;

- (a) oxo; or
(b) thial

R^3 is:

- 30 (a) $-S(O)_2-CH_3$;
(b) $-S(O)_2-NH_2$;

- (c) $-\text{S}(\text{O})_2-\text{N}(\text{H})-\text{C}(\text{O})-\text{CF}_3$;
- (d) $-\text{S}(\text{O})(\text{NH})-\text{NH}_2$;
- (e) $-\text{S}(\text{O})(\text{NH})-\text{CH}_3$;
- (f) $-\text{S}(\text{O})(\text{NH})-\text{N}(\text{H})-\text{C}(\text{O})-\text{CF}_3$;
- (g) $-\text{S}(\text{O})_2$ -haloalkyl; or
- (h) $-\text{CH}_2-\text{U}-\text{V}$;

R^4 is:

- (a) hydrogen;
- (b) substituted lower alkyl
- (c) cycloalkyl
- (d) cycloalkylalkyl;
- (e) lower alkenyl;
- (f) lower alkoxy;
- (g) alkylcarbonyl;
- (h) carboxylic ester;
- (i) carboxamido;
- (j) arylcarbonyl;
- (k) alkylsulfonyl;
- (l) arylsulfonyl;
- (m) alkylarylsulfonyl; or
- (n) arylalkylsulfonyl;

R^5 is:

- (a) hydrogen; or
- (b) lower alkyl; or

R^4 and R^5 taken together with the nitrogen to which they are attached form a heterocyclic ring;

R^6 is:

- (a) lower alkyl; or
- (b) arylalkyl;

R^7 is:

- (a) hydrogen;

- (b) halo;
(c) cyano;
(d) lower alkyl optionally substituted with:

- (1) halo;
(2) alkoxy;
(3) aryloxy;
(4) cycloalkoxy;
(5) ester;
(6) carbamoyl;
(7) $-NR^4R^5$;
(8) phenyl optionally substituted with:
(i) halo;
(ii) hydroxy;
(iii) lower alkyl; or
(iv) alkoxy;
(9) cyano;
(10) $-C(O)-H$
(11) alkylcarbonyl;
(12) carboxylic ester;
(13) carboxamido; or
(14) heterocyclic ring;

(e) haloalkyl;

(f) lower alkenyl optionally substituted with:

- (1) cyano;
(2) $-C(O)-H$
(3) alkylcarbonyl;
(4) arylcarbonyl;
(5) $-C(O)-cycloalkyl$;
(6) $-C(O)-heterocyclic\ ring$;
(7) carboxylic ester;
(8) nitro; or

- (9) $-NR^4R^5$;
- (g) nitro;
- (h) $-NR^4R^5$;
- (i) $-S(O)_6R^9$;
- 5 (j) $-S(O)_6NR^5R^{10}$;
- (k) $-C(O)-H$;
- (l) alkylcarbonyl;
- (m) arylcarbonyl;
- (n) $-C(O)-\text{cycloalkyl}$;
- 10 (o) $-C(O)-\text{heterocyclic ring}$;
- (p) carboxylic ester;
- (q) carboxamido;
- (r) alkoxy;
- (s) aryloxy;
- 15 (t) cycloalkoxy;
- (u) ester;
- (v) carbamoyl; or
- (w) $-D$

R^9 is:

- 20 (a) lower alkyl;
- (b) haloalkyl;
- (c) phenyl; or
- (d) benzyl;

R^{10} is:

- 25 (a) hydrogen;
- (b) lower alkyl;
- (c) aryl;
- (d) cycloalkyl;
- (e) cycloalkylalkyl;
- 30 (f) lower alkenyl; or
- (g) lower alkoxy;

R¹¹ is:

- (a) lower alkyl;
- (b) lower haloalkyl;
- (c) alkoxyalkyl;
- (d) alkylcarbonyl;
- (e) arylalkylcarbonyl;
- (f) carboxamido; or
- (g) arylcarbonyl;

R¹² is:

- (a) lower alkyl;
- (b) hydrogen; or
- (c) -C(O)H;

R¹³ is:

- (a) hydrogen;
- (b) halogen;
- (c) lower alkyl;
- (d) lower alkoxy; or
- (e) lower haloalkyl;

a is an integer equal to 1 or 3;

b is an integer equal to 2 or 3;

o is an integer from 0-2;

D is -W_k-E_l-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-U-V;

wherein c, d, g, i, j, k and l are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently:

- (a) -C(O)-;
- (b) -C(S)-;
- (c) -T-;
- (d) -(C(R_e)(R_f))_h-;
- (e) alkyl;
- (f) aryl;

- (g) heterocyclic ring;
- (h) arylheterocyclic ring, or
- (i) $-(\text{CH}_2\text{CH}_2\text{O})_q-$;

E at each occurrence is independently:

- 5 (a) -T-;
- (b) alkyl;
- (c) aryl;
- (d) $-(\text{C}(\text{R}_e)(\text{R}_f))_h-$;
- (e) heterocyclic ring;
- 10 (f) arylheterocyclic ring; or
- (g) $-(\text{CH}_2\text{CH}_2\text{O})_q-$;

h is an integer from 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently:

- 15 (a) hydrogen;
- (b) alkyl;
- (c) cycloalkoxy;
- (d) halogen;
- (e) hydroxy;
- 20 (f) hydroxyalkyl;
- (g) alkoxyalkyl;
- (h) arylheterocyclic ring;
- (i) alkylaryl;
- (j) cycloalkylalkyl;
- 25 (k) heterocyclicalkyl;
- (l) alkoxy;
- (m) haloalkoxy;
- (n) amino;
- (o) alkylamino;
- 30 (p) dialkylamino;
- (q) arylamino;

	(r) diarylamino;
	(s) alkylaryl amino;
	(t) alkoxyhaloalkyl;
	(u) sulfonic acid;
5	(v) alkylsulfonic acid;
	(w) arylsulfonic acid;
	(x) arylalkoxy;
	(y) alkylthio;
	(z) arylthio;
10	(aa) cyano;
	(bb) aminoalkyl;
	(cc) aminoaryl;
	(dd) aryl;
	(ee) arylalkyl;
15	(ff) alkylaryl;
	(gg) carboxamido;
	(hh) alkylcarboxamido;
	(ii) arylcarboxamido;
	(jj) amidyl;
20	(kk) carboxyl;
	(ll) carbamoyl;
	(mm) alkylcarboxylic acid;
	(nn) arylcarboxylic acid;
	(oo) alkylcarbonyl;
25	(pp) arylcarbonyl;
	(qq) ester;
	(rr) carboxylic ester;
	(ss) alkylcarboxylic ester;
	(tt) arylcarboxylic ester;
30	(uu) sulfonamido;
	(vv) alkylsulfonamido;

- (ww) arylsulfonamido;
 (xx) sulfonic ester;
 (yy) urea;
 (zz) nitro; or
 5 (aaa) $-(C(R_e)(R_f))_k-U-V$; or
 R_e and R_f taken together with the carbon to which they are attached are:
 (a) oxo;
 (b) thial;
 (c) aryl;
 10 (d) heterocyclic ring;
 (e) cycloalkyl group; or
 (f) bridged cycloalkyl group;
 U is:
 (a) oxygen;
 15 (b) sulfur; or
 (c) $-N(R_a)R_i-$;
 V is:
 (a) $-NO$; or
 (b) $-NO_2$;
 20 T at each occurrence is independently:
 (a) a covalent bond,
 (b) carbonyl,
 (c) an oxygen,
 (d) $-S(O)_o-$; or
 25 (e) $-N(R_a)R_i-$;
 R_a is:
 (a) a lone pair of electron;
 (b) hydrogen; or
 (c) lower alkyl;
 30 R_i is:
 (a) hydrogen;

- (b) alkyl;
(c) aryl;
(d) alkylcarboxylic acid;
(e) aryl carboxylic acid;
5 (f) alkylcarboxylic ester;
(g) arylcarboxylic ester;
(h) alkylcarboxamido;
(i) arylcarboxamido;
(j) alkylaryl;
10 (k) alkylsulfinyl;
(l) alkylsulfonyl;
(m) arylsulfinyl;
(n) arylsulfonyl;
(o) sulfonamido;
15 (p) carboxamido;
(q) carboxylic ester;
(r) aminoalkyl;
(s) aminoaryl;
(t) $-\text{CH}_2-\text{C}(\text{U}-\text{V})(\text{R}_e)(\text{R}_f)$; or
20 (u) $-(\text{N}_2\text{O}_2)^-\cdot\text{M}^+$, wherein M^+ is an organic or inorganic cation.
2. The compound of claim 1, wherein at least one substituent in the compound contains a “-U-V” moiety, wherein U and V are as defined herein.
3. A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.
- 25 4. A composition comprising the compound of claim 2 and a pharmaceutically acceptable carrier.
5. A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 3.
- 30 6. A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount

of the composition of claim 3.

7. The method of claim 6, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendonitis, bursitis, a skin-related condition, neoplasia, inflammation in disease, ophthalmic disorder, pulmonary inflammation, central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, inflammation, microbial infection, cardiovascular disorder, urinary disorder, urological disorder, endothelial dysfunction, a disorder treated by the preservation of organs and tissues, a disorder treated by inhibition of activation, adhesion and infiltration of neutrophils at the site of inflammation, or a disorder treated by inhibition of platelet aggregation.

8. A method for treating a gastrointestinal disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 4.

9. The method of claim 8, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, a hypersecretory state associated with systemic mastocytosis or basophilic leukemia or hyperhistaminemia.

10. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 4.

11. The method of claim 10, wherein the wound is an ulcer.

12. A method for treating or reversing renal toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 4.

13. A method for improving the cardiovascular profile of a COX-2 selective inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 4.

14. The method of claim 13, further comprising administering to the patient a therapeutically effective amount of at least one of a 3-hydroxy-3-methylglutaryl coenzyme A, an antiplatelet agent, a thrombin inhibitor or a thromboxane inhibitor.

15. A method for improving the cardiovascular profile of a COX-2 selective inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of at least one the compound of claim 2, or a pharmaceutically acceptable salt thereof, and at least one of a 3-hydroxy-3-methylglutaryl coenzyme A, an antiplatelet agent, a thrombin inhibitor or a thromboxane inhibitor.

16. The method for claim 15, wherein the compound of claim 2 or a pharmaceutically acceptable salt thereof, and the least one of a 3-hydroxy-3-methylglutaryl coenzyme A, an antiplatelet agent, a thrombin inhibitor or a thromboxane inhibitor are administered separately or are administered together in the form of a composition.

17. The method of claim 16, wherein the compound of claim 2 or a pharmaceutically acceptable salt thereof, and the least one of a 3-hydroxy-3-methylglutaryl coenzyme A, an antiplatelet agent, a thrombin inhibitor or a thromboxane inhibitor are administered orally, buccally, topically, by injection, by inhalation, or by transdermal application.

18. A composition comprising at least one compound of claim 1 or a pharmaceutically acceptable salt thereof, and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and, optionally, at least one therapeutic agent.

19. The composition of claim 18, further comprising a pharmaceutically acceptable carrier.

20. The composition of claim 18, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

21. The composition of claim 20, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione, or S-nitroso-cysteinyl-glycine.

22. The composition of claim 20, wherein the S-nitrosothiol is:

(i) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{SNO}$;

(ii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{R}_e$; or

(iii) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_m-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an

alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, a cycloalkylalkyl, a heterocyclicalkyl, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an alkoxy, an aryl, an arylalkyl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, an arylsulfonyloxy, a carbamoyl, a urea, a nitro, -T-Q-, or $(C(R_e)(R_f))_k$ -T-Q, or R_e and R_f taken together are an oxo, a methanthial, a heterocyclic ring, a cycloalkyl group or a bridged cycloalkyl group; Q is -NO or -NO₂; and T is independently a covalent bond, a carbonyl, an oxygen, -S(O)_o- or -N(R_a)R_i-, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, -CH₂-C(T-Q)(R_e)(R_f), or -(N₂O₂-)•M⁺, wherein M⁺ is an organic or inorganic cation; with the proviso that when R_i is -CH₂-C(T-Q)(R_e)(R_f) or -(N₂O₂-)•M⁺; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group.

23. The composition of claim 18, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine, lysine, polypeptides comprising at least one of these amino acids or inhibitors of the enzyme arginase.

24. The composition of claim 18, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a NONOate.

25. The composition of claim 18, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-

derived relaxing factor, or is a substrate for nitric oxide synthase is:

- (i) a compound that comprises at least one ON-O-, ON-N- or ON-C- group;
- (ii) a compound that comprises at least one O₂N-O-, O₂N-N-, O₂N-S- or -O₂N-C- group;

5 (iii) a N-oxo-N-nitrosoamine having the formula: R¹R²N-N(O-M⁺)-NO, wherein R¹ and R² are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M⁺ is an organic or inorganic cation.

10 26. The composition of claim 25, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-O-polypeptide, an ON-N-polypeptide, an ON-C-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-C-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-C-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-C-hydrocarbon, an ON-O-heterocyclic compound, an ON-N-heterocyclic compound or a ON-C-heterocyclic compound.

20 27. The composition of claim 25, wherein compound comprising at least one O₂N-O-, O₂N-N-, O₂N-S- or O₂N-C- group is an O₂N-O-polypeptide, an O₂N-N-polypeptide, an O₂N-S-polypeptide, an O₂N-C-polypeptide, an O₂N-O-amino acid, O₂N-N-amino acid, O₂N-S-amino acid, an O₂N-C-amino acid, an O₂N-O-sugar, an O₂N-N-sugar, O₂N-S-sugar, an O₂N-C-sugar, an O₂N-O-oligonucleotide, an O₂N-N-oligonucleotide, an O₂N-S-oligonucleotide, an O₂N-C-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-S-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-C-hydrocarbon, an O₂N-O-heterocyclic compound, an O₂N-N-heterocyclic compound, an O₂N-S-heterocyclic compound or an O₂N-C-heterocyclic compound.

28. The composition of claim 18, wherein the therapeutic agent is a steroid, a

nonsteroidal antiinflammatory compound, a 5-lipoxygenase inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H₂ receptor antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

29 The composition of claim 3, further comprising at least one therapeutic agent.

30 The composition of claim 29, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H₂ receptor antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

31 A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 18 or 29.

32 A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 18 or 29.

33 The method of claim 32, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendonitis, bursitis, a skin-related condition, neoplasia, inflammation in disease, ophthalmic disorder, pulmonary inflammation, central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, inflammation, microbial infection, cardiovascular disorder, urinary disorder, urological disorder, endothelial dysfunction, a disorder treated by the preservation of organs and tissues, a disorder treated by inhibition of activation, adhesion and infiltration of neutrophils at the site of inflammation, or a disorder treated by inhibition of platelet aggregation.

34. A method for treating a gastrointestinal disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 18 or 29.

35. The method of claim 34, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, a hypersecretory state associated with systemic mastocytosis or basophilic leukemia or hyperhistaminemia.

36. A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 18 or 29.

37. The method of claim 36, wherein the wound is an ulcer.

38. A method for treating or reversing renal toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 18 or 29.

39. A method for improving the cardiovascular profile of a COX-2 selective inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 18.

40. The method of claim 39, further comprising administering to the patient a therapeutically effective amount of at least one of a 3-hydroxy-3-methylglutaryl coenzyme A, an antiplatelet agent, a thrombin inhibitor or a thromboxane inhibitor.

41. The composition of claim 18, wherein the least one compound of claim 1 or a pharmaceutically acceptable salt thereof and the least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase are administered separately or are administered together in the form of a composition.

42. The composition of claim 18, wherein the least one compound of claim 1 or a pharmaceutically acceptable salt thereof, the least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and the at least one therapeutic

agents are administered orally, buccally, topically, by injection, by inhalation, or by transdermal application.

43. A kit comprising at least one compound of claim 1 or a pharmaceutically acceptable salt thereof.

44. The kit of claim 43, further comprising at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

45. The kit of claim 43, further comprising at least one therapeutic agent.

46. A kit comprising at least one compound of claim 1 or a pharmaceutically acceptable salt thereof, and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

47. The kit of claim 46, wherein the compound of claim 1 or a pharmaceutically acceptable salt thereof, and the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase are separate components in the kit or are in the form of a composition in the kit.

48. A kit comprising at least one compound of claim 1 or a pharmaceutically acceptable salt thereof, and at least one therapeutic agent.

49. The kit of claim 48, wherein the compound of claim 1 or a pharmaceutically acceptable salt thereof, and the at least one therapeutic agent are separate components in the kit or are in the form of a composition in the kit.

50. A compound selected from 4-(1-(3',5'-difluorophenyl)-1-hydroxymethyl)-1,2-dimethoxy-5-(methylsulfonylphenyl) benzene, 5-(1-(3',5'-difluorophenyl)methyl)-1,2-dimethoxy-4-(4-methylsulfonylphenyl)benzene, 5-(1-(3',5'-difluorophenyl)methyl)-1,2-dihydroxy-4-(4-methylsulfonylphenyl)benzene, 4-(1-(3',5'-difluorophenyl)-1-oxomethyl)-1,2-dimethoxy-5-(4-methylsulfonylphenyl)benzene, 4-(1-(3',5'-difluorophenyl)-1-oxomethyl)-1,2-hydroxy-5-(4-methylsulfonylphenyl)benzene, 1-(2-(cyclohexylidenemethyl)phenyl)-4-(methylsulfonyl)benzene, 1-(2-((3-fluorophenyl)hydroxymethyl)phenyl)-4-(methylsulfonyl)benzene, 3-fluorophenyl 2-(4-(methylsulfonyl)phenyl)phenyl ketone, 1-(2-((3-fluorophenyl)methyl)phenyl)-4-(methylsulfonyl)benzene, or a pharmaceutically acceptable salt thereof.

51. A composition comprising at least one compound of claim 50 and a pharmaceutically acceptable carrier.

52. A kit comprising at least one compound of claim 50.

53. A composition comprising at least one compound of claim 50 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, and, optionally, at least one therapeutic agent.

54. A composition comprising at least one compound of claim 50 and at least one therapeutic agent, and, optionally, at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.